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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,633	02/23/2004	Tomoyuki Shirai	671302-2004	1513
20999	7590	08/10/2005	EXAMINER	
FROMMER LAWRENCE & HAUG 745 FIFTH AVENUE- 10TH FL. NEW YORK, NY 10151			LIETO, LOUIS D	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/784,633	SHIRAI ET AL.	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 February 2004 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/07/2005</u> | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Claims 1-9 are currently under examination. An action on the merits follows.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35

U.S.C. 119(a)-(d). It is noted that while applicant has filed certified copies of International Application PCT/JP02/08373 and WO 06/017756 A1, English translations of these documents has not been provided.

Information Disclosure Statement

The information disclosure statement filed On 2/23/2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. None of the listed references have been submitted. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

Claim 2 and 3 are objected to because of the following informalities: A connexon is a structure made up of six connexin proteins; the grammar of the claims does not make this clear. Appropriate correction is required.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

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The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because the grammar and language is awkward almost to the point of complete unintelligibility. For example, the abstract refers to "make it possible to detect a carcinogen highly sensitively." It is suggested that the submitted abstract is a machine translation and has not been edited to conform to proper English grammar. Correction is required. See MPEP § 608.01(b).

Drawings

The drawings are objected to under 37 CFR 1.83(a) because they fail to show the histological details as described in the specification. Specifically, the resolution and clarity of Figure 3 is so poor as to make it impossible to discern the structural details. Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. Any amended replacement-drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets

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may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the examiner does not accept the changes, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims encompass a wild-type rat whose normal function in a gap junction is inhibited, and does not require the intervention of the hand of man. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable the Artisan to make and/or use the invention. The invention appears to employ novel biological materials, i.e., the Tg-H high

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expressor rat (Specification pg. 7-8, Example 2). Applicant has disclosed that 5 rats were made that contained the transgene, and that four of them transmitted the transgene to next generation, of which only two expressed the deletion mutant Cx32 mRNA in the liver, and only one, Tg-H, was verified to display the claimed phenotype (Specification pg. 7-8, Example 2). Similarly, applicant's published results indicate that only one founder rat line (Cx32 Δ Tg-high) of the five made showed inhibition of endogenous Cx32 throughout the liver {Asamoto et al. (2004) Hepatology 40:205-210; pg. 207, col. 1, pgphs 1&2}. Therefore, the method of making the claimed rat is sensitive to positional effects that completely or partially repress expression of the transgene leading to an abrogation of the phenotype. Houdebine et al., states that "numerous experiments have shown that the level and specificity of expression of a gene construct used as a transgene cannot be easily predicted" {Houdebine et al. (2000) Transgenic Research 9:305-320; pg. 309, col. 2: The expression of transgenes}. See also Kolb et al., who states that "the expression of foreign genes in transgenic mammals is generally unpredictable as transgenes integrated at random after pro-nuclear injection into fertilized oocytes" because of inhibition by neighboring chromatin {Kolb et al. (1999) Gene 227:21-31; Abstract}.

Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or otherwise available, the requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. If the deposit is made under the Budapest treaty, then an affidavit or declaration by Applicant, or a

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statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon issuance of a patent would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to MPEP §2400 in general, and specifically to §2411.05, as well as to 37 CFR § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims encompass any rat, wild-type or transgenic whose normal gap junction function is inhibited for any reason, wherein the inhibition may be do to a deficiency in connexon function, such as a mutation in connexin 32. Further, the claims encompass a method of making a transgenic rat by pro-nuclear injection of a plasmid vector engineered to carry mutated rat connexin downstream of a promoter into a fertilized egg, wherein the promoter may be an albumin promoter. Wherein the rat may be used to detect a carcinogen or screen for an anti-cancer substance.

Applicant should note that upon fulfillment of the requirements for biological deposit, as set forth above, the specification only provides a limited enablement of the claimed invention. The specification discloses a transgenic rat whose genome comprises a connexin 32 (Cx32) mutant transgene, comprising the sequence of SEQ ID NO.3 operably linked to the albumin promoter, wherein the transgene is expressed in a liver specific manner in male rats, wherein the transgenic rat has greater sensitivity to a carcinogen then a wild-type rat and shows increased hepatocarcinogenesis in response to exposure to a carcinogen, compared to a wild-type rat. A method of making the rat via pro-nuclear injection with the Cx32 mutant transgene, comprising the sequence of SEQ ID NO.3 operably linked to the albumin promoter mutant transgene, and a method for detecting a carcinogen, and a method of screening an anti-cancer substance in said male transgenic rat.

The claims broadly read on any rat sensitive to a carcinogen with inhibited gap junction function. This would include any rat with a transgene or endogenous disruption that inhibits gap junction function. However, the specification only provides guidance on the making and using of a transgenic Cx32 dominant-negative rat (Example 1 and Example 5). Wherein the transgene encodes a dominant negative deletion mutant Cx32 protein lacking amino acids in the 113th to the 124th position of the protein, under the control of an albumin promoter. The albumin promoter is a liver specific promoter. Therefore, the dominant negative Cx32 protein is only expressed in the liver of the disclosed rat and cannot inhibit gap junction function in any other tissue. The specification does not provide any guidance on making or using any transgene other than a dominant negative Cx32 mutant transgene, with the sequence of SEQ ID NO.3 operably linked to the albumin promoter, which is capable of producing the claimed phenotype in a rat. Neither the specification nor the art of record indicates that expression of a dominant negative Cx32 mutant transgene under the control of any other tissue specific promoter can produce a phenotype wherein carcinogenesis is induced in a tissue other than the liver. Dominant negative mutants work by inhibiting the action of the wild type protein and can do so in a heterozygous fashion. However, applicant's published disclosure describing their invention indicates that for unknown reasons: "female transgenic rats were found to express very little mRNA of the transgene regardless of a high copy number in the genomic DNA; these rats also demonstrated a similar Cx32 immunostaining pattern to that of the wild type." {Asamoto et al. (2004) Hepatology 40:205-210; pg. 207, col. 1, pgphs 1&2}. For this reason only male rats were used in the experiments described in the publication of Asamoto et al. Therefore the practitioner in the art would not predict that female rats could be used in any method of detecting carcinogens or

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screening anticancer substances because of their failure to express the transgene and display a phenotype different from a wild type rat.

The prior art of record describes that mice deficient for Cx32 have a higher incidence of spontaneous and chemically induced tumors in the liver than wild-type control mice (Temme et al. (1997) *Current Biology* 7:713-716). Temme et al. states that tumors were not observed in organs other than the liver in Cx32 knockout mice (pg. 713, col.2, pgph 3). Therefore, the skilled practitioner would not predict that tumors would be observed in any organ, other than the liver, in the disclosed dominant negative Cx32 mice. However, neither the prior art of record nor the specification provides any guidance on how to make a connexin 32 knockout rat. For example, guidance as to the specific sequences to be targeted in the rat in order to produce the claimed phenotype. The art of transgenics and making knockout animals is quite complex, requires intimate knowledge about the precise sequences to be used and/or targeted and is unpredictable based on sequence alone.

The state of the art of transgenics is not a predictable art with respect to transgene behavior and the resulting phenotype. While the art of transgenics is such that one of skill in the art would be able to produce a transgenic rat comprising any transgene of interest, it is not predictable if the transgene would be expressed at a level and specificity sufficient to cause a particular phenotype. For instance, the level and specificity of expression of a transgene as well as the resulting phenotype of the transgenic rat are directly dependent on the specific transgene construct. The individual gene of interest, promoter, enhancer, coding, or non-coding sequences present in the transgene construct, the vector used, and the specific site of transgene integration into the genome (positional effect), for example, are all important factors in controlling the

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expression of a transgene in the production of transgenic mammal which exhibits a resulting phenotype. These issues become even more complicated when working with more than one transgene, especially when the products of one transgene regulate the expression of the other. This observation is supported by Houdebine et al., who states that “numerous experiments have shown that the level and specificity of expression of a gene construct used as a transgene cannot be easily predicted” {Houdebine et al. (2000) *Transgenic Research* 9:305-320; pg. 309, col. 2: The expression of transgenes}. Further, Houdebine et al. states that the potency of any transgene can only be estimated in transgenic mammals and the level of expression of transgenes in mice is not predictive of their levels in other mammals (pg. 310, col. 1, pgph 2). Finally, Houdebine et al. states that another well known problem with transgenesis is leaky expression of the transgene in various tissues in which the utilized promoter is not expected to work because of ectopic expression due to a position effect (pg. 310, col.1, pgph 3). See also Kolb et al., who states that “the expression of foreign genes in transgenic mammals is generally unpredictable as transgenes integrated at random after pro-nuclear injection into fertilized oocytes” because of inhibition by neighboring chromatin {Kolb et al. (1999) *Gene* 227:21-31; Abstract}.

The art of making any transgenic rat, other than the disclosed dominant negative Cx32 mutant transgenic rat, is not predictable because of several factors. Well-regulated transgene expression is the key to successful transgenic work, but all too often experiments are blighted by poor levels or the complete absence of expression, as well as less common problems, such as leaky expression in non-targeted tissues. A feature common to many transgenic experiments is the unpredictable transgenic lines produced with the same construct frequently displaying different levels of expression. Further, expression levels do not always correlate with the

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number of transgene copies integrated {Leiter et al. (2002) *Diabetologia* 45:296-308;pg. 304, col. 1}. Such copy- number-independent expression patterns emphasize the influence of surrounding chromatin on the transgene (pg. 303, col. 2). Additionally, promoters and enhancer elements may not function in any species because they may require specific cellular factors. The background genotype of the rodent strain used can have a drastic effect on the phenotype of the transgenic rodent. Lariviere et al. teaches that the 129 and C57BL/6 mouse strains, despite having the same null mutation “display significant and sometimes extreme phenotypic differences.” {Lariviere et al. (2001) *J. Pharm. And Exp. Therap.* 297:467:473; Abstract}. The specification does not disclose that any transgene comprising any deletion or mutation of the Cx32 can express a dominant negative protein that will produce the claimed phenotype. Further, applicant has disclosed that 5 rats were made that contained the transgene, and that four of them transmitted the transgene to next generation, of which only two expressed the deletion mutant Cx32 mRNA in the liver, and only one, Tg-H, was verified to display the claimed phenotype (Specification pg. 7-8, Example 2). Similarly, applicant’s published results indicate that only one founder rat line (Cx32ΔTg-high) of the five made showed inhibition of endogenous Cx32 throughout the liver {Asamoto et al.; pg. 207, col. 1, pgphs 1&2}. Given the unpredictability of making the claimed rat as demonstrated by applicant’s difficulty in making a rat with the claimed phenotype applicant has only provided a disclosure that enables the Tg-H rat.

Given the lack of guidance disclosed in the specification on how to make the broadly claimed rat, the lack of teachings in the art on how to make any Cx32 transgene that encoded a dominant negative protein and the teachings in the art on the general unpredictability of making any transgenic animal, the skilled practitioner would be unable to predict how to practice the

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claimed invention, except as for a transgenic Cx32 dominant-negative rat that has greater sensitivity to a carcinogen than a wild-type rat, a method of making the rat via pro-nuclear injection, wherein the dominant negative Cx32 mutant transgene, comprises the sequence of SEQ ID NO.3 operably linked to the albumin promoter, and a method of screening an anti-cancer substance.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Hully et al.

{Hully et al. (1994) Am. J. of Pathology. 145: 384-397}.

Hully et al. provides guidance on a transgenic rat whose normal gap junction function is inhibited by an absence of Cx32 in all lesions of the transgenic animal (Abstract). Specifically, Hully et al. teaches the development of a strain of transgenic rats that carry a transgene comprising a mouse albumin promoter linked 5' to the SV40 T antigen gene (Abstract, p5. 385, materials and methods). Wherein, the rat developed hepatocarcinomas that completely lack expression of Cx32 (Abstract; pg. 394, col.2, pgph 2 thru pg. 395, col.1 pgph 1). It is inherent that a lack of Cx32 expression inhibits normal gap junction function. Thus, by teaching all the limitations of the claims as written, Hully et al. anticipate the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5,7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omori et al. {Omori et al. (June 2001) Mutation Research 477:191-196}, in view of Lukkarinen et al. {Lukkarinen et al. (1997) Stroke 28:639-645} and Eghbali et al. {Eghbali et al. (1990) Proc. Natl. Acad. Sci. 87:1328-1331}.

Omori et al. provides guidance on the development of a transgenic mouse that comprises a transgene encoding a dominant-negative Cx32 mutant expressed under the control of a liver specific albumin gene promoter in which Cx32 expression is down-regulated only in the liver (Abstract). Specifically, wherein the transgene used to make the mouse comprises a V139M mutant Cx32 gene driven by a liver specific albumin promoter. Further, Omori et al. teaches a method of detecting a carcinogen in mouse comprising administering diethylnitrosamine to the transgenic mouse and wild-type mice (pg. 194, col.1, pgph 2). Omori et al. does not teach making a transgenic rat by pro-nuclear injection using a mutated rat Cx32 nucleic acid sequence.

Lukkarinen et al. supplements the guidance of Omori et al. by teaching the production of transgenic rats by the standard technique of pro-nuclear injection (pg. 3, Materials and Methods).

Eghbali et al. supplements the guidance of Omori et al. by teaching a plasmid DNA containing the rat connexin 32 cDNA insert, used for transfection and expression in mammalian cells (Abstract; pg. 1328, col.2, Materials and Methods).

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Based on the guidance provided by Omori et al. on a method of making a dominant-negative Cx32 mutant transgenic mouse, the guidance of Lukkarinen et al. on the standard technique of pro-nuclear injection and the guidance of Eghbali et al. on a rat connexin 32 cDNA, it would be *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Omori et al. by making a dominant-negative rat Cx32 mutant transgene using the Cx32 taught by Eghbali et al. to make a transgenic rat by pro-nuclear injection. Further it would be *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the transgenic rat to detect a carcinogen, such as diethylnitrosamine, and to use the rat in a method of screening for an anti-hepatocarcinoma substance.

A practitioner in the art would be motivated to modify the method of Omori et al. with the teachings of Eghbali et al. and Lukkarinen et al. in order to produce a dominant-negative Cx32 mutant transgenic rat, which could be directly compared to chemical models of hepatocarcinogenesis in rats.

The person of ordinary skill in the art would have a reasonable expectation of success because using the teachings of Omori et al. with the rat Cx32 sequence of Eghbali et al. to make a transgenic rat using the technique taught by Lukkarinen et al. would have been a routine modification in the art at the time of filing.

No claims Allowed.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier


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communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Dr. Louis D. Lieto
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